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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,721	06/25/2001	James S. Huston	P 23,611-A USA	2094

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EXAMINER

LIETO, LOUIS D

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 08/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

9/888,721

Applicant(s)

HUSTON ET AL.

Examiner

Louis D. Lieto

Art Unit

1632

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 29 June 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☒ The Notice of Appeal was filed on 05 July 2006. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-8, 16, 20-22, 26 and 29.

Claim(s) withdrawn from consideration: 9-15, 17-19, 23-25, 27, 28 and 30-52.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

*Anne-Marie Falk*

ANNE-MARIE FALK, PH.D.  
PRIMARY EXAMINER

Continuation of 3. NOTE: The claims filed on 6-26-06 require further search and consideration because the claims have been amended so as that they are drawn to a broader range of subject matter than those previously under consideration. Therefore they will not be entered.

Continuation of 11. Other: Applicant's arguments are presented in regards to the claims of 6-26-06. However since these claims were not entered the claims submitted on 10-05-05 remain pending.

#### Claim Rejections - 35 USC § 112

The rejection of claims 1-8, 16, 20-22, 26 and 29 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. This rejection is based on applicant's inclusion of new matter in the claims of 10-05-06. This rejection is maintained for reasons of record as set forth in the office action of 12/29/05.

The rejection of claims 1-8, 16, 20-22, 26 and 29 under 35 U.S.C. 112, first paragraph, is maintained, because the specification, while being enabling for a gene delivery compound comprising a single chain binding polypeptide and a nucleic acid binding moiety, wherein the compound comprises the C6ML3-9 sFv'SP conjugate, which binds to cells expressing the erbB2 surface marker to deliver a tumor suppressor gene in vitro, does not reasonably provide enablement for a gene delivery compound comprising a single chain binding polypeptide and a nucleic acid binding moiety, wherein the compound comprises the C6ML3-9 sFv'SP conjugate, which binds to cells expressing the erbB2 surface marker to deliver a tumor suppressor gene to any cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant argues that the examiner appears to base his rejection on the fact that claimed conjugate can only bind erB2, and that this is irrelevant. Applicant argues that sFv molecules may be based on antibodies that bind to antigens other than erB-2. It is noted that applicant has not provided any guidance on how the claimed compound is to do so when the specification only discloses compounds capable of gene delivery by binding to erb2. Applicant is reminded that the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Therefore the rejection is maintained for reasons of record as set forth above and in the prior actions of 4-05-05 and 12-29-05.

#### Claim Rejections - 35 USC § 103

The rejection of claims 1-8, 16, 20-22, 26 and 29 under 35 U.S.C. 103(a), is maintained, as being unpatentable over Wagner et al. {Wagner et al. (1990) Proc. Natl. Acad. Sci. USA 87:3410-3414}, further in view of US Patent No. 5,977,322, hereafter referred to as Marks et al. and of International Patent Application No. WO 00/04922, hereafter referred to as Konadu et al.

Applicant argues that there is no motivation for combining the cited references to produce the claimed invention. However, it is well established in case law that a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. In re Burkel, 201 USPQ 67 (CCPA 1979). Furthermore, in the determination of obviousness, the state of the art as well as the level of skill of those in the art are important factors to be considered. The test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). For the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references. In re Nilssen, 7 USPQ2d 1500 (Fed. Cir. 1988). Further obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See In re O'Farrell, 7 USPQ2d 1673 (CAFC 1988). As previously stated: One of ordinary skill in the art would have been motivated by the teachings of Marks et al. that C6ML3-9 sFv can be used to specifically bind to tumor cells, to modify the C6ML3-9 sFv by cross linking it with salmon protamine taught by Wagner et al. in order to deliver a therapeutic tumor suppressor gene sequence to the specifically to the tumor cells in order to treat cancers that express erbB-2. The gene delivery compound containing the salmon protamine taught by Wagner can be used to deliver any nucleic acid sequence, including any tumor suppressor gene. It would be obvious to the skilled artisan to use any heterobifunctional cross linking agent, such as the SMCC taught by Konadu et al., to crosslink the salmon protamine to the C6ML3-9 sFv. Therefore the rejection is maintained for reasons of record as set forth above and in the prior actions of 4-05-05 and 12-29-05.